# Exhibit C

**IN THE UNITED STATES DISTRICT COURT**
**FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA**
**CHARLESTON DIVISION**

| | |
|---|---|
| **IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION**<br><br>**THIS DOCUMENT RELATES TO: WAVE 5 TVT/TVT-O CASES** | **Master File No. 2:12-MD-02327**<br>**MDL No. 2327**<br><br>**JOSEPH R. GOODWIN**<br>**U.S. DISTRICT JUDGE** |

# GENERAL REPORT OF

# RAGNVALD MJANGER, M.D.

Prepared by

Ragnvald Mjanger, M.D.

June 14, 2017

# GENERAL REPORT OF RAGNVALD MJANGER, M.D.

## TVT and TVT-O Devices

## I. Background and Qualifications

My curriculum vitae is enclosed and it provides additional information regarding my background and qualification. (Attachment A). Continuously since December 2000, I have been board certified in Obstetrics and Gynecology. I am also board-certified in Female Pelvic Medicine and Reconstructive Surgery (also sometimes referred to as Urogynecology), as of June 2015. I am an inaugural Fellow in the subspecialty. I am currently a partner with Premier ObGyn (formerly known as Metro ObGyn, PA), St. Paul, Minnesota, a private clinical practice where I focus on obstetrics and gynecology and female pelvic medicine and reconstructive surgery.

From 2004 to present, I have been an Assistant Clinical Professor at the University of Minnesota Medical School. I have also served as the chair or vice chair of various Obstetrics and Gynecology departments and have been a member of and chaired a peer review committee in obstetrics and gynecologic surgery, respectively.

I was initially trained in obstetrics and gynecology and began to specialize in pelvic reconstructive surgery after I began treating women with incontinence issues in the late 1980s. I have treated thousands of women with incontinence since 1988 and I have performed over 10,000 pelvic surgeries including many different types of procedures to treat stress incontinence: open and laparoscopic retropubic urethropexies, including Burch and Marshall-Marchetti-Krantz (MMK) procedures, needle suspensions, fascial bladder neck slings, and synthetic mid-urethral slings. I have used retropubic, obturator and single incision sling approaches. I am familiar with the potential risks and complications associated with all non-operative treatments and also with surgical incontinence procedures. I have participated in professional education from Ethicon for TVT, TVT-O and TVT-Exact.

I have served as a preceptor for Ethicon in cadaver labs and as a preceptor in the Operating Room, teaching slings and mesh procedures to other physicians. I regularly attend continuing medical education conferences, some of which deal with surgery for stress urinary incontinence and other pelvic floor disorders. I have given community lectures about the treatment of urinary incontinence and pelvic organ prolapse. I have also lectured for doctors about robotic surgery and pelvic organ prolapse. I currently teach robot assisted laparoscopic and minimally invasive gynecologic surgery to gynecologists, urologists and residents.

## II. Materials Reviewed

Materials that I have reviewed are citied in this report and attached along with materials which I may use at trial. (Attachment B). All of my opinions are held to a reasonable degree of medical and scientific certainty. I have also reviewed the Plaintiffs' expert reports and the materials cited by Plaintiffs' experts. I reserve the right to amend and provide additional opinions as additional information becomes available and following the depositions of the experts for Plaintiffs.

## III. Testimonial History

Karen Swanson and Thomas Swanson v. Johnson & Johnson, et al., MDL, Case No. 2:12-cv-01709, May 12 2016 (treating physician).

## IV. Disclosure of Opinions

All of my opinions are based on my education, training, professional experience, and review of the medical and scientific literature. They are also a reflection of my annual participation in continuing medical education courses. All of my opinions are held to a reasonable degree of medical and scientific certainty. In summary, in my opinion, the TVT and TVT-O designs are reasonably safe for their intended use, no other design or mesh has been demonstrated to be more effective, safer, or has been studied as much, as long, or in as many patients and types of patients as the TVT has showing it is safe and effective and the TVT and TVT-O IFU are adequate to warn of the risks of the TVT and TVT-O devices discussed below.

### A. Urinary Incontinence

Urinary incontinence or the involuntary leakage of urine affects women of all ages. The reported incidence varies depending on the study, and may vary depending on population studied, method of recording leaks and the definition of leakage used by the authors. Currently, best estimates are that accidental leakage of urine affects 10 -55% of women on a regular basis.

One way to define the type of accidental urine leakage is by using patient symptoms. The following are symptom-based definitions:

Stress urinary incontinence (SUI) refers to accidental leakage of urine that occurs with physical stress on the bladder, such as with coughing, sneezing, jumping, standing, or lifting a heavy object. In extreme cases, stress leakage can occur simply as a result of a change in position, or can even become continuous.

Urge urinary incontinence (UUI) refers to sudden leakage, usually of large amounts of urine, preceded by a warning or an urge to urinate. Women with mixed incontinence experience symptoms of both stress incontinence and urge incontinence.

Overactive Bladder (OAB) refers to a constellation of symptoms, including urgency, frequency, urge incontinence, and nocturia (the need to pass urine at night).

SUI is often first identified when a patient complains that she is losing urine during stress events (i.e., coughing, sneezing, and exercising). These stress events cause intra-abdominal pressure that leads to leading in the absence of detrusor contraction. SUI can be confirmed by physical examination (Q-tip test, Valsalva) and urodynamic studies.

In general terms, women with SUI have a combination of weak ligament support and weak pelvic muscles. Other factors include increased abdominal pressure, such as that which occurs with chronic coughing and obesity; or inherently weak periurethral tissues or a loss of elasticity of the urethra so that there is no coaptation of the urethral walls. A more severe form of SUI is known as Intrinsic Sphincteric Deficiency (ISD). ISD is defined as Low Leak Point Pressure as

measured on urodynamic testing, most commonly under 60 cmH2O. Drainpipe urethra implies a urethral lumen that does not close, even at rest, with lack of hypermobility of the urethra. Hypermobility or an excursion of the urethral angle greater than 30 degrees with strain or cough implies weak ligamentous support of the urethra.

Known risk factors for stress urinary incontinence include: advancing age, pregnancy/childbirth, obesity, genetic predisposition/ethnic heritage, menopausal status, diabetes, kidney disease, smoking, chronic coughing and other factor.

Urinary incontinence negatively affects a patient's quality of life. The leakage is bothersome, causes odors and embarrassment, and can lead to isolation behaviors. Women who suffer from urinary incontinence score low on Quality of Life (QOL) questionnaires and may experience depression. (Fantl JA, et al. Urinary incontinence in adults: acute and chronic management. Clinical practice guideline. Vol. 2, Rockville (MD); US Department of Health and Human Services. Public Health Service, Agency for Health Care Policy and Research, 1996)

Options for treating SUI include behavioral treatments, non-surgical treatments and surgical procedures. Behavioral methods include weight loss, control of chronic cough, decreasing fluid intake and timed voiding. Non-surgical treatments include pelvic muscle (Kegel) exercises, with or without aid of a pelvic floor physical therapist, biofeedback devices or intravaginal electrical stimulation, an intravaginal incontinence pessary (a device worn in the vagina that externally compresses the urethra), urethral caps (Capsure®), urethral inserts (Femsoft®) and possibly timed voiding. There are no FDA-approved prescription medications to treat SUI. Behavior modification and non-surgical intervention have limited success in the treatment of SUI and generally only benefit patients with minimally bothersome symptoms.

Procedures or surgeries to treat SUI include injection or periurethral bulking agents, mid-urethral synthetic mesh slings, cadaveric fascia or autologous fascia pubovaginal slings, or abdominal retropubic urethropexy, including the Marshall-Marchetti-Kranz Procedure (MMK) and the Burch procedure.

### B. Historical Treatment of SUI

SUI has been surgically managed since 1907. At that time, the procedure was done with the gracilis muscle.[1] Pubovaginal sling surgery, as we think of it today, was introduced in 1978 using rectus fascia.[2] That operation involved both abdominal and vaginal incisions. The rectus fascia was harvested through an abdominal incision and implanted through a vaginal incision. Although the success rate of the technique was initially good, these results declined over time. This procedure, as well as the MMK procedure and the Burch procedure, were the most common procedures used to treat SUI before the 1990s.

The MMK procedure is also known as a retropubic suspension or bladder neck suspension surgery. This procedure involves general anesthesia, requires a 2-6 day hospital stay, can lead to

[1] Giordano D. Guerison par autoplastie musculo-nerveuse d'une incontinence vesicale, suite de "befida spina'. Cong. Frac De Chir 1907, 28:84

[2] McGuire, EJ, Lytton B. Pubovaginal sling procedure for stress incontinence. J. Urol. 1978; 119(1):82.

bony or other pelvic complications, and has inferior long-term efficacy. The MMK procedure is not the procedure of choice today and is not even taught in residency programs any more.

The Burch procedure originated in the 1960s. In this procedure, surgeons attach the paravaginal fascia to Cooper's ligaments. The Burch procedure requires an abdominal incision, is time-consuming, and requires a prolonged rehabilitation. Because of the significant post-operative morbidity, voiding difficulty, de novo pelvic organ prolapse, pain and delayed failures, the Burch procedure has also lost popularity with surgeons.

In 2002, the Burch colposuspension was compared to MUS using TVT and the results proved the non-inferiority from one procedure compared to the other, with follow-up lasting to five years.[3] In 2004, laparoscopic Burch colposuspension was compared to TVT with mean follow up of 20.6 months and the results showed shorter operating time for TVT and that the TVT also leads to greater objective and subjective cure rates for urodynamic stress incontinence than does laparoscopic Burch colposuspension.[4] TVT has been found to have shorter operative time and hospital stay, and higher objective urodynamic cure than laparoscopic Burch colposuspension,[5] as well as significantly less de novo urgency incontinence and time to return to daily activities.[6]

A 2007 study published by the Urinary Incontinence Treatment Network ("UITN") compared outcomes for patients who underwent the Burch procedure to outcomes for patients who underwent a sling procedure. The study, titled the SISTEr trial, concluded that "success rates were higher for women who underwent the sling procedure than for those who underwent the Burch procedure." More recently, longer term data from the SISTEr trial were published. Continence rates at 5 years were Burch 24.1% versus Fascial sling 30.8% (p=0.002 in favor of Fascial sling). (Brubaker 2012 J. Urology). In fact, at seven years, the urinary continence rate was only 13% for patients who underwent the Burch procedure and was 27% for patients who underwent the sling procedure. (Richter 2012 J. Urology). This study is not without limitations. For example, patients in the sling group experience more frequent voiding dysfunction and retention when compared to patients who underwent the Burch procedure. The pubovaginal sling (PVS) procedure places graft material directly under the urethra and attaches it to the connective tissue (fascia) of the abdominal muscles or to the pelvic bone. The success rate of the sling is good, but long-term success rates may show some decline. In comparison to the Burch, the fascial sling has a higher rate of UTI, urge incontinence, voiding dysfunction and the need for surgical revision to improve voiding, such as urethrolysis to relieve urethral obstruction. The increased efficacy but greater morbidity of the fascial sling is echoed in other systematic reviews and in my own practice and experience.

C. **Transition to Mesh to Treat SUI**

[3] Ward K, Hilton P on behalf of the UK and Ireland TVT Trial Group. Prospective multicenter randomized trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. BMJ 2002; 325:67; Ward K, Hilton P on behalf of the UK and Ireland TVT Trial Group. Tension-free vaginal tape versus colposuspension for primary urodynamic stress incontinence: 5-year follow up. BJOG 2008; 115:226-233.
[4] Paraiso MF, Walters MD, Karram MM, Barber MD. Laparoscopic Burch colposuspension versus tension-free vaginal tape: a randomized trial. Obstet Gynecol. 2004 Dec; 104(6):1249-58.
[5] Dean N, Herbison P, Ellis G, Wilson D. Laparscopic colposuspension and tension-free vaginal tape: a systematic review. BJOG. 2006 Dec; 113(12):1345-53.
[6] Ogah J, Cody DJ, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women: a short version Cochrane review. Neurourol Urodyn. 2011 Mar; 30(3):284-91.

The Gynecare TVT, and others in its family, is made from Prolene (polypropylene) mesh. Surgeons have used polypropylene mesh as a permanent human implant for decades. The first meshes were developed and used by hernia surgeons in the 1950s. Ethicon started using Prolene (polypropylene and certain extracts) in sutures in the 1960s. Prolene sutures have been used for various procedures including cardiovascular repairs, plastic surgery, hernia repairs and pelvic floor repairs. Ethicon used the same material to develop Prolene mesh for hernia surgery in the early 1970s.

In the 1990's, Dr. Ulmsten, along with Dr. Peter Petros, began placing several different types of mesh under the mid-urethra to treat SUI.[7] The surgeons experimented with, among others, Prolene, Gore-Tex, and Mersilene. Prolene demonstrated the most promising results. Eventually, Dr. Ulmsten began placing meshes loosely around the urethra, a procedure that became the TVT procedure.

Dr. Ulmsten's first trial concluded in 1996 and included 75 patients with a two-year follow-up.[8] Of those 75 patients, 84% (63 patients) were completely cured and an additional 8% (6 patients) were significantly improved. None of these patients experienced significant intra- or postoperative complications, defective healing, or rejection of the sling.

In 1997, Ethicon began to sell TVT in Europe. In 1998, several surgeons, including Dr. Ulmsten, carried out a prospective randomized study with six centers in Scandinavia to test the safety and efficacy of the TVT device. The study included 131 patients suffering from SUI. Of those 131 patients, 91% (119 patients) were cured and another 79% (9 patients) saw significant improvement.[9]

Since 1998, the literature has substantially supported TVT's safety and efficacy. In fact, well over 100 randomized controlled trials have assessed the TVT and over 1,000 studies have addressed the TVT mesh.[10]

### D. **Gynecare's TVT**

Polypropolene mesh slings, such as the TVT, are the most common surgical treatment for SUI. The extensive published studies demonstrate minimal morbidity compared with alternative surgeries such as Burch, MMK or PVS. Advantages of the midurethral sling procedure include shorter operative time/anesthetic need, smaller incisions, reduced surgical pain, reduced

---

[7] Petros, PE, Ulmsten UI (1993), An integral theory and its method for the diagnosis and management of female urinary incontinence. *Scan J Urol Nephrol Suppl*; 153: 1-93; Ulmsten U, et al., A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct* 1998; 9(4):210-3; Petros P. (2015). Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond: Ulf Ulmsten Memorial Lecture. *Int Urogynecol J* 26(4):471-76.

[8] Ulmsten, U, et al. (1996) An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. *Int Urogynecol J* 7:81-86.

[9] Ulmsten U (1998) A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. *Int Urogynecol J*, 9:210-213.

[10] A systematic review of patient-years of experience in prospective randomized controlled trials (RCTS) in incontinence, ETH.MESH.07246690-719; CERT VT Family of Products, ETH.MESH.10178882-10179216.

hospitalization, reduced voiding dysfunction, higher long-term success rates, and low complications.[11]

Although mesh-related complications can occur following polypropylene sling placement, the rate of these complications is acceptably low. Furthermore, most sling-related complications such as urinary retention, UTI, and pelvic pain occur with mesh and non-mesh procedures.[12]

1. *TVT Has Been Widely Studied*

There are hundreds of Randomized Controlled Trials with TVT and others in its family (TVT-O, TVT-S, etc., as well as those from other companies) establishing their efficacy and safety, including numerous long term studies evaluating the TVT and TVT-O. These studies demonstrative objective and subjective cure rates for 80-95% of patients.[13]

Dr. Carl Nillson published 17-year data for the TVT in 2013.[14] Dr. Nilsson reported data for 46 women who were followed postoperatively for 17 years. Of those 46 women, 91.3% (42 women) were objectively cured. These women showed no clinically significant contracture, no tape rejection, and only one mesh exposure, which was asymptomatic and due to vaginal atrophy in an elderly patient who was satisfied with the outcome. This study demonstrated the TVT is safe and effective after 17 years. Dr. Nilsson also noted that no mesh shrinkage with the TVT

[11] American Urological Association, Position Statement of the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence, October 2013.

[12] FDA, Considerations About Surgical Mesh for SUI, April 2, 2013. U.S. Food and Drug Administration http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/UroGynSurgicalMesh/ucm345219.htm; American Urological Association, Position Statement on the Use of Vaginal Mesh Treatment of Stress Urinary Incontinence, October 2013.

[13] Nilsson CG et al. (2008) Eleven years prospective follow-up of the tension-free vaginal tape procedure for treatment of stress urinary incontinence. *Int Urogynecol J* 19:1043-47; Liapis A, et al. (2008) Long-term efficacy of tension-free vaginal tape in the management of stress urinary incontinence in women: efficacy at 5-and 7-year follow-up. *Int Urogynecol J*, 19:1509-12; Olsson I et al. (2010 Long-tern efficiacy of the tension-free vaginal tape procedure for the treatment of urinary incontinence. *Int. Urogynecol J* 21:679-83; Liapis A et al. (2010) Efficacy of inside-out transobturator vaginal tape (TVTO) at 4 years follow up. *Eur J Obstet Gynecol Reprod Biol* 148:199-201. Angioli R, et al. (2010) Tension-free vaginal tape versus transobturator suburethral tape: five-year follow-up results of a prospective, randomised trial. *Eur Urol* 48:671-77; Groutz A, et al. (2011) Ten-year subjective outcome results of the retropubic tension-free vaginal tape for treatment of stress urinary incontinence. *J Minim Invasive Gynecol* 18(6):726-729; Aigmueller T, et al. (2011) Ten year follow-up after the tension-free vaginal tape procedure. *Am J Ostet Gynecol* 205:496; Groutz A, et al. (2011) Long-term outcome of transobturator tension-free vaginal tape: efficacy and risk factors for surgical failure. *J Womens Health* 20(10):1525-28; Cheng D, Liu C (2012) Tension-free vaginal tape obturator in the treatment of stress urinary incontinence: a prospective study with five-year follow-up. *Eur J Obstet Gynecol Reprod Biol* 161(2):228-31; Heinonen P, et al. (2012) Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. *Int J Urol* 19(11):1003-09; Serati M, et al. (2012) Tension-free vaginal tape for the of urodynamic stress incontinence: efficacy and adverse effects at 10-year follow-up. *Eur Urol* 61:939-46; Nilsson CG, et al. (2013) Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J* 24:1265-69; Svenningsen R (2013) Long-term follow-up of the retropubic tension-free vaginal tape procedure. *Int. Urogynecol J* 24:1271-78; Serati M, et al. (2013) TVT-O for the treatment of pure urodynamic stress incontinence: efficacy, adverse effects, and prognostic factors at 5-year follow-up. *Eur Urol* 63:872-78; Laurikainen E et al. (2014) supra; Athanasiou S et al. (2014) Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: why do tapes fail? *Int Urogynecol J* 25:219-25.

[14] Nilsson CG et al. (2013) Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J* 19:1043-47.

was observed at 17 year follow-up. In an earlier three-center prospective observational study by Dr. Nilsson (2008), he reported that at 11.5 years, 90% of the 90 women were objectively cured and 77% were subjectively cured.[15] Another 20% of the patients were improved. Only 3% of the patients considered the operation to be a failure. Notably, there were no late-onset adverse effects and there was no erosion. In that study, Dr. Nilsson concluded that "[t]he TVT procedure is safe and effective for more than 10 years." In an even earlier prospective long-term, multicenter study (2001), Dr. Nilsson reported that 84.7% (72) of 85 patients were both objectively and subjectively cured five years after their implants.[16] There were no long-term voiding difficulties and no signs of defective healing or rejection of the tape material. Dr. Nilsson's long term and consistent results clearly demonstrate the long-term safety and effectiveness of TVT.

The TVT is the most effective procedure for women because it provides a well-known and well-established treatment for SUI. It is minimally invasive and safer when compared to alternative procedures, including the Burch procedure and autologous pubovaginal slings. This is further demonstrated in several meta-analyses (Cochrane review), systematic reviews, and guidelines.

Polypropylene mid-urethral slings have been and continue to be the gold standard for treatment of SUI. No other device or SUI surgery has been studied as extensively as TVT. Contrary to Plaintiffs' experts' claims, TVT's long term results clearly demonstrate that complications associated with TVT do not increase over time. TVT is the safest procedure.

I am aware that Plaintiffs' experts have opined that procedures including anterior plications, needle suspension, MMK and open and laparoscopic Burch colposuspensions are safer alternative procedures when compared to the TVT. These procedures are considered native tissue repairs, but do require the use of a permanent suture such as Prolene or Gore-Tex. It is well accepted now that anterior plications, need suspension (such as the Raz procedure), paravaginal defect repair, and the MMK are not considered first line treatment options for SUI. The success rates are lower and the risks are more serious than MUS.[17]

There is no 100% safe or effective surgical procedure. TVT and TVT-O are medical devices to aid surgeons in obtaining good results for their patients, results which are at least as effective and as safe as the alternatives. Although not applicable here, sometimes a slight increase in risk might even be outweighed by an increase in efficacy, depending on patient characteristics and other factors. Those are decisions best left to discussions between the doctor and patient. TVT and TVT-O are not "defective products just because some patients develop complications from either the surgical process, or the mesh itself. Again, and in short, TVT and TVT-O have been proven safe and effective in the treatment of SUI, and carry no more risk, or less efficacy, than the available alternative treatments. The clinically relevant, potential risks of SUI surgery,

---

[15] Nilsson CG et al. (2008) Eleven years prospective follow-up of the tension-free vaginal tape procedure for treatment of stress urinary incontinence. *Int Urogynecol J* 19:1043-1047.

[16] Nilsson CG et al. (2001) Long term results of the tension free vaginal tape (TVT) procedure for surgical treatment of female stress urinary incontinence. *Int. Urogynecol J* (Suppl 2):S5-S8.

[17] National Institute for Health and Care Excellence, Urinary incontinence: The management of urinary incontinence in women, Sept. 2013 at guidance.nice.org.uk/cg171; American Urological Association, Position Statement on the Use of Vaginal Mesh for Surgical Treatment of Stress Urinary Incontinence, October 2013; American College of Obstetricians and Gynecology, Practice Bulletin Summary, 126 (5), November 2015.

including with TVT and TVT-O, are well-known to pelvic surgeons through several sources, and are adequately warned of in the product materials.

E. **Alleged Complications Associated with TVT**

Plaintiffs' experts claim that TVT is associated with several complications, including infection, chronic inflammation that leads to pain, cytotoxicity, shrinking, contraction, pore collapse, degradation, roping, curling, particle loss, complications that occur due to the cut of the mesh, and cancer. Those claims are not supported with evidence-based studies, nor have I observed them in my clinical experience. The 2014 Schimpf systematic review performed by the SBS and the 2015 Ford Cochrane Review provide an excellent resource in the peer reviewed literature for level 1 evidence regarding complication rates associated with synthetic midurethral slings, such as TVT.

- Infection: Infection rates are very low at less than 1%. Also, Ethicon, through the TVT IFU, warns of the possibility of infection when implanting a TVT device. The IFU also warns that removal may be necessary in some cases of persistent infection. Infections are no more common with TVT mesh than they are with native tissue repairs. Furthermore, any infection can usually be treated without removal of the mesh.[18]

- Inflammation: Plaintiff's experts have suggested that there may be an inappropriate inflammatory response associated with the TVT. In my practice, I have not experienced a chronic inflammatory response with TVT that resulted in clinical consequences such as pain. Nor is it demonstrated in the literature from peer-reviewed urology, urogynecology, or gynecology journals. It is known and accepted that there will be some level of inflammatory response with any foreign body. In my experience this inflammation remains stable, or contained in an area immediately adjacent to the mesh, and does not continue to expand in size. I have also found that this degree of inflammation is not clinically harmful or significant and is rarely associated with any adverse effects.

- Cytotoxicity: Any claim that TVT is cytotoxic in women is not credible. The long-term studies and data do not show cytotoxicity, and their results are contrary to Plaintiffs' experts' theories, which rely on in vitro testing. A study by Wang and colleagues upon which they rely reporting a rate of persistent defective healing of 1%, has not been replicated in other clinical studies in women. Ethicon extensively studied cytotoxicity and its results satisfied FDA that the mesh was not cytotoxic.

[18] Amin P, et al. (1994) Biomaterials and Abdominal Wall Hernia Surgery, Inguinal Hernia: Advances or Controversies, Radcliffe Medical Press; Amin P, et al. (1997) Classification of biomaterials and their related complications in abdominal wall hernia surgery, Hernia (1997) 1:15-21; FDA Polypropylene Reclassification Letter, July 5, 1990.

- Contraction: Contrary to Plaintiffs' experts' contention, in my experience, TVT mesh does not curl, rope, shrink, contract, or experience pore collapse when implanted as directed in the IFU. A close analysis of literature contending that mesh contracts reveals that it is the tissue around the mesh that contracts, *not the mesh*. If contraction occurs at some unseen level, it is not clinically significant. Scar tissue contracts in any pelvic surgery. If the TVT mesh had significant contracture, it would contract uniformly, chronically elevating the bladder and leaving almost all patients with voiding dysfunction. The clinical literature again does not support these propositions. In fact, there is no level 1 evidence to indicate that contraction is a clinically relevant phenomenon. Clinically significant tissue contraction is a rare complication, but can occur with any pelvic floor surgery, including but not limited to incontinence and prolapse surgeries as well as hysterectomies.

- Degradation: Plaintiffs' experts claim that TVT degrades in vivo. Although pathology studies have reported mixed data on degradation, a close review of that literature reveals that degradation, if it occurs at all, is not clinically significant. For example, the Clave study reported on 100 explants that were studied under the SEM. Only 42% of the specimens showed any degradation at all. Other studies, including by Dr. Dmochowski, showed no degradation in the synthetic slings. Thus degradation is clearly not a universal finding. Clinical evidence, including my own clinical experience, established that TVT mesh does not degrade in vivo. If it does, any such degradation does not lead to any clinically significant effect that one would theorize, such as a high failure rate of the TVT. Any degradation, if it does occur, does not lead to recurrence, pelvic pain, or dyspareunia. Instead, long-term clinical studies show lasting success and low to no late-term complications. Plaintiffs' experts often confuse particle loss and microscopic degradation. I have examined TVT upon removal and have never noticed any mesh that appeared degraded or had loose particles. I have reviewed the clinical literature extensively and have never seen any reliable scientific studies showing clinically significant consequences such as pain that were attributable to theorized particle loss or degradation. In fact, even in the Clave study, which Plaintiffs' experts suggest is indicative of in vivo degradation, the authors could not conclusively confirm any degradation in the majority of their specimens.

- Cancer: There is no reliable scientific information to support Plaintiffs' experts' claim that polypropylene can cause cancer or sarcoma. Medical literature is devoid of reports of tumors related to the implantation of surgical-grade polypropylene for midurethral slings. In fact, recent

published studies from the Mayo and Cleveland Clinics show no association between polypropylene MUS and cancer.[19]

- Urinary Tract Infections (UTI): There is no scientific evidence showing that TVT increases the risk of urinary tract infections. While it is feasible for a TVT midurethral mesh procedure to make a patient more susceptible to a UTI, the circumstances are unusual: retention or incomplete bladder emptying, or an extrusion of mesh into either the bladder or urethra. Otherwise, the presence of mesh outside the urinary tract, where it is supposed to be placed, does not cause UTIs.

I am aware that there are mechanically versus laser cut mesh products. Based on my experience, and from the literature, there is no difference between laser-cut versus mechanically cut mesh from a clinical standpoint. They perform the same. The data from 1998 to 2006 (before laser-cut mesh was available) is consistent with the data from 2006 to the present (when laser-cut mesh was available), showing similar efficacy and safety in hundreds of studies, randomized controlled trials and reviews. The data show no difference in exposures over time.

Moreover, Plaintiffs' experts often say that TVT and TVT-O, both mechanically cut mesh and laser cut mesh, are defective in that they contribute to an increased likelihood of erosions. This opinion is not consistent with my own clinical experience or the medical literature. A review of the medical literature before laser cut mesh was introduced to the market in 2007 and afterwards shows that there is no difference in the range or rate of complications or in the overall effectiveness of the products. This confirms Ethicon's own internal finding when they compared laser and mechanically cut mesh and found no clinical difference between the two within the physiological range of forces that would be exerted at the mid-urethra.

### F. Official Guidelines from Governmental Agencies or Medical Societies Regarding SUI surgery and Slings

Several governmental agencies and medical societies have published guidelines or reports about the safety of mesh used in stress urinary incontinence procedures. These agencies include the American Urogynecologic Society ("AUGS")[20], the Society of Urodynamics and Female Urology ("SUFU"), IUGA, the America Urological Association ("AUA"), the Food and Drug Administration ("FDA"), and the National Institute for Health and Care Excellence ("NICE"), ACOG, EAU, MHRA, and the EU Commission SCHEHNIR Report. Many of these entities

[19] Moore C, et al. (2014) Is There an Association Between Polypropylene Midurethral Slings and Malignancy? *Female Urology* 84(4), 2014; Moalli P, et al. (2014), Polypropylene mesh: evidence for lack of carcinogenicity. *Int Urogynecol J* DOI 10.1007/s00192-014-2343-8; King AB, et al. (2014) Current controversies regarding oncologic risk associated with polypropylene midurethral slings. *Curr Urol Rep* 15: 453; Sunoco MSDS; AUGS & SUFU, Frequently Asked questions by Providers – Mid-urethral Slings for Stress Urinary Incontinence. (available at http:/www.augs.org/pbl/et/blogaid=194); King AB et al. (2014), Is there an association between polypropylene MVS and malignancy? *Urology* 84:789-792; Linder B, et al. (2016) Evaluation of local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. *Int Urogynecol J* DOI 10.1007/s00192-016-2961-4.

[20] American Urogynecologic Society and Society or Urodynamics and Female Urology joint position statement on midurethral slings; American Urogynecologic Society Position Statement on Restrictions of Surgical Options for Pelvic Floor Disorders, March 2013.

have published various statements advocating the use of synthetic midurethral slings in the treatment of Stress Urinary Incontinence in women. Prominent organizations, like those listed above, appoint committees of highly-respected urologists and urogynecologists to draft position statements on areas of interest, such as the surgical management of stress urinary incontinence.

For example, FDA published a statement in 2013. There, the FDA concluded, based on an earlier review of the medical literature, that "[t]he safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year."

The AUA published its own position statement in November 2011 (and revised it in October 2013)[21], where it concluded that "[e]xtensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries." Based on extensive data, "the AUA Guideline for the Surgical Management of Stress Urinary Incontinence (2009) concluded that synthetic slings are an appropriate treatment choice for women with stress incontinence, with similar efficacy but less morbidity than conventional non-mesh sling techniques."

In November 2015, AUGS/ACOG published a Practice Bulletin on women with urinary incontinence "to review information on the current understanding of urinary incontinence in women and to outline guidelines for diagnosis and management that are consistent with the best available scientific evidence." There, AUGS and ACOG made the following conclusions:

- "Initial midurethral sling surgery results in higher 1-year subjective and objective cure rates than pelvic floor physical therapy in women with stress urinary incontinence."

- "Synthetic midurethral slings demonstrate efficacy that is similar to traditional suburethral fascial slings, open colposuspension, and laparoscopic colposuspension."

- "Compared with suburethral fascial slings, fewer adverse events have been reported with synthetic midurethral slings. Voiding dysfunction is more common with open colposuspension than with synthetic midurethral slings. There are substantial safety and efficacy data that support the role of synthetic mesh midurethral slings as a primary surgical treatment option for stress urinary incontinence in women."

In 2014, AUGS and SUFU published a position statement "to support the use of the midurethral sling in the surgical management of stress urinary incontinence." This statement was updated in 2016. There, AUGS and SUFU made several key points:

1) "[p]olypropylene material is safe and effective as a surgical implant";

[21] American Urological Association, Position Statement of the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence, November 2011; American Urological Association, Update to the Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence, October 2013.

2) "[t]he monofilament polypropylene mesh MUS is the most extensively studies anti-incontinence procedure in history";

3) "[p]olypropylene mesh midurethral slings are a standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients";

4) "[t]he FDA has clearly stated that the polypropylene MUS is safe and effective in the treatment of SUI."

In conclusion, the position statement aptly notes that "[t]he polypropylene midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly.

I agree with each of these statements.

## G. **The TVT Warnings Are Sufficient**

### 1. *Instructions for Use*

I have been a preceptor for MUS professional education for Ethicon. The professional education curriculum and availability of preceptors and learning opportunities were well planned, thorough and went beyond industry norms. Surgery and potential risks were discussed. During these activities, I did didactic lectures, instructed in cadaver labs, proctored physicians who observed my cases in my operating room, observed surgeons on their first cases in their operating rooms and taught on the IFU. I believe that the IFU is adequate in providing information concerning the potential risks of the TVT and TVT-O to the intended users, namely pelvic floor surgeons who perform SUI surgery. The IFU further states that surgeons should undergo the professional education, which supplements the IFU. It is not a comprehensive treatise on pelvic floor surgery. Our education, training, experience and continuing medical education provide to us the knowledge to perform pelvic floor surgery. As pelvic floor surgeons, we know the potential risks of SUI surgery and the only unique risk with the MUS is mesh exposure, although would complications and suture erosions occur with non-mesh SUI surgeries. The basic elemental risks with SUI surgery are taught to us during training, learned by reading medical literature, in practicing clinically, discussed in professional capacities at meetings, and studied in connection with professional medical education and our certification process.

I am familiar with Instructions for Use (IFU) generally from my experience in the use of medical devices. I have reviewed IFUs for many medical devices. I have been able to compare my own surgical experience, as well as, that published in the medical literature, to the list of potential risks contained in IFUs. I am familiar with the information commonly included in IFUs, as well as information commonly excluded from IFUs. Relying on my experience, I am able to review the sufficiency of an IFU and to determine whether I need to affirmatively seek out additional information. Further, I am familiar with physicians' use of and reliance on IFUs.

I have reviewed the IFUs for both the TVT and the TVT-O. It is in my opinion, based on my years of clinical experience, training, discussions with colleagues, involvement with professional societies, experience teaching other surgeons how to interpret the IFU and perform various

surgical procedures, as well as handling complications after mesh surgeries, that the TVT and TVT-O IFUs fairly and adequately informs reasonable prudent pelvic surgeons of the indications for the TVT and TVT-O, the associated procedure, and the potential risks and complications.

An IFU is not intended to be a comprehensive training guide for the surgical treatment of SUI. Instead, surgeons operating within the standard of care should already be familiar with the risks, potential complications, and benefits associated with pelvic surgery, with or without mesh. The risks associated with these surgeries have been widely publicized in medical literature and at medical conferences. Additionally, the FDA has acknowledged that risks known to be common to pelvic floor surgery (even without mesh) include pain, infection, urinary problems, recurrent incontinence, pain during sexual intercourse (dyspareunia), bleeding, organ perforation, neuro-muscular problems and vaginal scarring.[22]

The TVT-O IFU specifically states, in two locations, that the TVT-O "should be used only by physicians trained in the surgical treatment of Stress Urinary Incontinence and specifically in implanting the GYNECARE TVT Obturator Device."[23] It further states that the "procedure should be performed with care to avoid large vessels, nerves, bladder and bowel" and that "[b]leeding may occur post-operatively."[24] It also warns that "de novo detrusor instability may occur following a sub-urethral sling procedure," that "[p]unctures or lacerations of vessels, nerves, bladder, urethra, or bowel may occur," that "[t]ransitory local irritation at the wound site and a transitory foreign body response may occur" which could "result in extrusion, erosion, fistula formation and inflammation," and that "[a]nimal studies show that implantation of PROLENE mesh elicits a minimal inflammatory reaction in tissues."[25] Of course a manufacturer could go further, if it wanted to, but complications such as pain and dyspareunia are not only potential complications of all SUI surgery, but are easily inferred when a surgeon knows he or she is making incisions into pelvic tissues, and is warned there could be damage to adjacent structures. All pelvic surgeons know that these complications can range in severity or duration.

I am aware that Ethicon updated the TVT and TVT-O IFUs in 2015, but those changes do not make the previous versions inadequate or misleading. All of these complications are well known, and have been for many years, and occur with any pelvic floor surgery as well as with the use of any implantable foreign body. I am not aware of IFUs in this industry that attach a specific rate for the incidence of a particular complication, as surgeons rely on the body of medical literature and their own clinical results for information about the frequency and severity of complications.

2. *Patient Brochure*

I have also reviewed the patient brochures for the TVT and TVT-O and find that they accurately described the condition of stress urinary incontinence and the procedures to treat SUI. I will testify that the patient brochures adequately convey basic information to the lay person and

[22] FDA, Considerations About Surgical Mesh for SUI, April 2, 2013. U.S. Food and Drug Administration http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/UroGynSurgicalMesh/ucm345219.htm downloaded June 13, 2017.
[23] ETH.MESH.02340902-908 at 903, 907.
[24] Id. at 907.
[25] Id. at 908.

recommend that the patient discuss her condition and options with her surgeon. Importantly, a patient brochure is not intended to replace the patient-surgeon relationship and informed consent process. Only a trained surgeon knows whether a particular patient's background, history, presentation, both and options are in the exercise of our medical judgment, and our discussion of the potential benefits and risks of options comes from our education, training, experience, our discussions with colleagues, attendance at professional meetings and the medical literature.

3. *Professional Education*

I have reviewed the professional education materials offered to surgeons by Ethicon in relation to their pelvic mesh products, and it is my opinion that Ethicon adequately apprised physicians practicing pelvic reconstructive surgery of the risks associated with the TVT and TVT-O, and that risks associated with these products were adequately described in their respective IFUs and other professional education materials.

**My Summary**

Based on my training, review of the literature, my clinical experience, among other things, I am in agreement with the statements, analyses and guidelines reviewed above. Synthetic midurethral slings are clearly recognized as first line, gold standard and standard of care both in the U.S. and abroad.

I practiced medicine before synthetic midurethral slings became available. Earlier in my career, restoration of anatomy was used, such as paravaginal repair, and Kelly plication and the Burch procedure were used to treat incontinence. From my clinical work, slings have the highest rate of curing incontinence, the most durable cure for incontinence, with the least complications and are very unlikely to result in non-treatable adverse symptoms.

In conclusion, the TVT and TVT-O, whether mechanically cut or laser cut, has been shown to be appropriately designed for the reasonably safe and effective use for treating female stress urinary incontinence. My opinions are supported by the vast body of level 1 peer-reviewed medical literature, which is consistent with my experience using the TVT products, as well as that of my colleagues, as reflected at CME conferences and in the office, as well as the major professional societies of our industry and the overseeing regulatory bodies.